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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/417,479	10/13/1999	JOHN MCCAFFERTY	2811/32729C	7504

7590 05/03/2006

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EXAMINER	
LUNDGREN, JEFFREY S	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/417,479	MCCAFFERTY ET AL.	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-53* is/are pending in the application.

4a) Of the above claim(s) *44-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election with traverse of Group II, claims 47-51, in the reply filed on October 12, 2000, is acknowledged. The traversal is on the grounds that the claims of Groups II-IV have been copied from U.S. Patent No. 5,849,500 to provoke an interference. Since the subject matter of Groups III and IV does not appear to present a serious search burden, Groups III and IV will be rejoined with Group II. Accordingly, claims 47-53 will be examined on the merits, while claims 44-46 are withdrawn from consideration as being drawn to a non-elected Group.

The requirement is deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on January 27, 2000; November 6, 2000; October 16, 2002; and July 30, 2003, have been considered by the Examiner. The submission is in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Objection to the Abstract Under 37 C.F.R. § 1.72

The abstract of the disclosure is objected to because it does not allow the public generally to determine quickly from a cursory inspection the nature and gist of the invention. Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should provide an abstract that describes each of the claim elements of at least one independent claim, such as claim 47. *See* 37 C.F.R. § 1.72. Should Applicants amend the claims in their next reply, the amended abstract should take into account any further limitations added to the broadest independent claim.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Great Britain. It is noted, however, that Applicants have not filed certified copies of the priority Applications as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 49 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 is indefinite for reciting the limitations "(SEQ ID NOS: 7-17) of FIGS 1(a)-1(c)." Based on a review of these SEQ ID NOS and Figures, it does not appear that these sequences properly correspond to the appropriate genetic elements, only that these limitations have been copied from U.S. Patent No. 5,849,500. Correction is required.

Claim Rejections - 35 USC § 112, first paragraph (New Matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It appears that the limitations "(SEQ ID NOS: 7-17) of FIGS 1(a)-1(c)" have been copied from U.S. Patent No. 5,849,500, but do not find support in the instant application. Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 53 is rejected under 35 U.S.C. 102(a) as being anticipated by Cwirla *et al.*, *Proc. Natl. Acad. Sci. USA 87*:6378-6382 (**1990**).

Claim 53 is directed to a method of presenting a peptide or protein at the surface of a phagemid viral particle, comprising producing said phagemid viral particle, wherein said phagemid viral particle comprises a DNA sequence encoding said peptide or protein fused to a DNA sequence encoding a contiguous full length coliphage pIII protein.

Cwirla teaches the construction of a library of phage displaying a library of hexapeptides and shows the vector fAFF1 in Fig. 1:

> "The adsorption protein, pIII, is made as a precursor protein with an 18-amino acid leader sequence that directs pIII to the inner membrane of the bacterial host cell before assembly into intact phage particles (17, 18). ***We constructed a peptide library by cloning oligonucleotides of the structure shown in Fig. 1 to place the variable hexapeptide region at the N terminus of the processed protein. These first six residues are followed by two glycine residues (as a flexible spacer) and then the normal sequence of pIII.*** The library consists of 3 x 108 independent recombinants recovered as tetracycline-resistant colonies; 72% of these produced infective phage."

Cwirla, at page 6379, col. 2, third full paragraph and refer to Fig. 1A and 1B (emphasis added). Accordingly, claim 53 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 47-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cwirla *et al.*, *Proc. Natl. Acad. Sci. USA 87*:6378-6382 (**1990**), in view of Dower *et al.*, U.S. Patent No. 5,427,908, issued on June 27, 1995, filed on May 1, 1990.

Claim 47 is directed to a phagemid comprising a DNA encoding a single-chain antibody-coliphage pIII fusion protein, wherein the fusion protein contains a contiguous full length coliphage pIII protein. Claim 50 is directed to a process of producing the phagemid vector of claim 47. Claim 48 is directed to the phagemid of claim 47, wherein the fusion has a protease sensitive region between the antibody and the coliphage pIII protein, and claim 51 is directed to the process of inserting a protease sensitive region into the phagemid. Claim 53 is directed to a method of presenting a peptide or protein at the surface of a phagemid viral particle.

Cwirla teaches the construction of a library of phage displaying a library of hexapeptides and shows the vector fAFF1 in Fig. 1:

> "The adsorption protein, pIII, is made as a precursor protein with an 18-amino acid leader sequence that directs pIII to the inner membrane of the bacterial host cell before assembly into intact phage particles (17, 18). ***We constructed a peptide library by cloning oligonucleotides of the structure shown in Fig. 1 to place the variable hexapeptide region at the N terminus of the processed protein. These first six residues are followed by two glycine residues (as a flexible spacer) and then the normal sequence of pIII.*** The library consists of 3 x 108 independent recombinants recovered as tetracycline-resistant colonies; 72% of these produced infective phage."

Cwirla, at page 6379, col. 2, third full paragraph and refer to Fig. 1A and 1B (emphasis added). The protease-sensitive region between the hexapeptide and the pIII coding region could be considered to protease-sensitive as in claims 48 and 51.

Although Cwirla teaches a phagemid having a hexapeptide-coliphage pIII protein, Cwirla does not explicitly teach that the inserted peptide should be a single chain antibody, as required in claim 47.

Dower teaches a method for the production of phagemid for expressing antibody fragments, such as single-chain antibodies:

> "Particularly preferred examples of such vectors are the filamentous phage fd, fl and M13. In this embodiment a library of DNA sequence members, each joined to a first nucleotide sequence coding for a tag protein, is cloned into an appropriate location of the phage genome, behind an appropriate promoter and translation sequences and a sequence encoding a signal peptide leader directing transport of the downstream fusion protein to the periplasmic space. The phage vector also contains a second DNA sequence inserted into a coat protein gene to express a tag ligand peptide acting as a ligand for the tag protein, which peptide is expressed in a location of the coat protein exposed to the external environment of the phage and, so, is accessible for binding by the tag protein. In a preferred embodiment this peptide is located ***at or near the N-terminus of the pIII coat protein***. The protein(s) of interest are expressed and transported to the periplasmic space, and the properly assembled proteins are adsorbed to the phage particle by virtue of the interaction of the tag protein with the ligand peptides on the phage as the phage particles are extruded from the cell. Phage bearing the desired protein are then selected by means of a ligand specific for the protein of interest."

Dower, at col. 2, lines 19-43 (emphasis added); and:

> "When the protein of interest is an antibody of a desired binding specificity, the ***antibody may be of any of the known isotypes or subclasses for a particular species, and may be a single-chain or two-chain binding complex or portion thereof***. For instance, only the variable antigen-binding regions of heavy (V_H) and/or light (V_L) chains may be identified and cloned; the binding fragments (F_v) or Fab encoded thereby may find use either as a binding fragment, joined to constant regions of heavy or light chains, or joined to other proteins having desired effector functions. The characteristics of the constant region domains will depend to a large extent on the use intended for the antibody, e.g., diagnostic and/or therapeutic applications, catalytic antibodies, etc."

Dower, at col. 3, lines 28-42 (emphasis added).

Both Cwirla and Dower teach producing phagemid by creating a fusion vector, as required by claim 50. Claim 52 is directed to a method of selecting antibodies from an antibody library comprising the screening using an antigen; this limitation is taught by Dower (col. 6, line 54 through col. 7, line 4).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because the teachings of each of Cwirla and Dower are directed towards compositions and methods for expressing certain proteins through coliphage at or near the pIII protein. One of ordinary skill in the art would have been motivated to utilize the antibody construction method of Dower for producing a library single-chain antibody fragments with the phagemid of Cwirla because the processing effects are not a severe limitation and would be useful in finding optimum antibody fragments towards a give antigen (Cwirla, at page 6382, cols. 1 and 2). Therefore, the invention as a whole, is *prima facie* obvious at the time it was invented.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 47-51 and 53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44-51 of copending Application No. 09/706,507. Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the claims are directed to essentially the same subject matter.

Claim 47 of the instant application is directed to a phagemid comprising a DNA encoding a single-chain antibody-coliphage pIII fusion protein, wherein the fusion protein contains a contiguous full length coliphage pIII protein; compare with claims 45 and 50 in the '507 application. Claim 50 is directed to the process of producing the phagemid; compare to claims 45, 48 and 50 in the '507 application. Claim 53 is directed to a method of presenting a peptide on the surface of a viral particle; compare to claim 48 of the '507 application.

Claim 48 is directed to the phagemid of claim 47, wherein the fusion has a protease sensitive region between the antibody and the coliphage pIII protein, and claim 51 is directed to the process of inserting a protease sensitive region into the phagemid; compare to claims 46, 48 and 51 in the '507 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 47-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44-51 of copending Application No. 09/706,507 in view of Dower *et al.*, U.S. Patent No. 5,427,908, issued on June 27, 1995, filed on May 1, 1990.

Claim 47 of the instant application is directed to a phagemid comprising a DNA encoding a single-chain antibody-coliphage pIII fusion protein, wherein the fusion protein contains a

contiguous full length coliphage pIII protein; compare with claims 45 and 50 in the '507 application. Claim 50 is directed to the process of producing the phagemid; compare to claims 45, 48 and 50 in the '507 application. Claim 53 is directed to a method of presenting a peptide on the surface of a viral particle; compare to claim 48 of the '507 application.

Claim 48 is directed to the phagemid of claim 47, wherein the fusion has a protease sensitive region between the antibody and the coliphage pIII protein, and claim 51 is directed to the process of inserting a protease sensitive region into the phagemid; compare to claims 46, 48 and 51 in the '507 application.

The claims in the '507 application do not recite the single chain antibody.

Dower teaches a method for the production of phagemid for expressing antibody fragments, such as single-chain antibodies:

> "Particularly preferred examples of such vectors are the filamentous phage fd, fl and M13. In this embodiment a library of DNA sequence members, each joined to a first nucleotide sequence coding for a tag protein, is cloned into an appropriate location of the phage genome, behind an appropriate promoter and translation sequences and a sequence encoding a signal peptide leader directing transport of the downstream fusion protein to the periplasmic space. The phage vector also contains a second DNA sequence inserted into a coat protein gene to express a tag ligand peptide acting as a ligand for the tag protein, which peptide is expressed in a location of the coat protein exposed to the external environment of the phage and, so, is accessible for binding by the tag protein. In a preferred embodiment this peptide is located ***at or near the N-terminus of the pIII coat protein***. The protein(s) of interest are expressed and transported to the periplasmic space, and the properly assembled proteins are adsorbed to the phage particle by virtue of the interaction of the tag protein with the ligand peptides on the phage as the phage particles are extruded from the cell. Phage bearing the desired protein are then selected by means of a ligand specific for the protein of interest."

Dower, at col. 2, lines 19-43 (emphasis added); and:

> "When the protein of interest is an antibody of a desired binding specificity, the ***antibody may be of any of the known isotypes or subclasses for a particular species, and may be a single-chain or two-chain binding complex or portion thereof***. For instance, only the variable antigen-binding regions of heavy (V_H) and/or light (V_L) chains may be identified and cloned; the binding fragments (F_v) or Fab encoded thereby may find use either as a binding fragment, joined to constant regions of

> heavy or light chains, or joined to other proteins having desired effector functions. The characteristics of the constant region domains will depend to a large extent on the use intended for the antibody, e.g., diagnostic and/or therapeutic applications, catalytic antibodies, etc."

Dower, at col. 3, lines 28-42 (emphasis added).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because the claims of the '507 and Dower are directed towards compositions and methods for expressing certain proteins through coliphage at or near the pIII protein. One of ordinary skill in the art would have been motivated to utilize the antibody construction method of Dower for producing a library single-chain antibody fragments with the phagemid of the '507 application because the advantages of producing antibody fragments towards a give antigen. Therefore, the invention is *prima facie* obvious.

This is a provisional obviousness-type double patenting rejection.

Conclusions

No claim is allowable.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

JON EPPERSON, PH.D.
PATENT EXAMINER